AMERICAN
ASSOCIATION
OF BLOOD BANKS

August 16, 1999

Dockets Management Branch (HFA- 305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: FDA Docket No. 99D-1878: Guidance for Industry Current Good Manufacturing Practice for Blood and Blood Components: (1) Quarantine and Disposition of Units from Prior Collections from Donors with Repeatedly Reactive Screening Tests for Antibody to Hepatitis C Virus (Anti HCV); (2) Supplemental Testing, and the Notification of Consignees and Blood Recipients of Donor Test Results for Anti HCV [Federal Register: June 22, 1999 (Volume 64, Number 119)].

To Whom it May Concern:

These comments are filed on behalf of the Interorganizational HCV Lookback Committee (Committee) created by the AABB to provide assistance to the blood banking community for HCV lookback. The members of the Committee represent the American Association of Blood Banks (AABB), America's Blood Centers (ABC), and the American Red Cross (ARC), and represent all of the blood collecting organizations and over 80% of the blood transfusion services in the United States. The Committee appreciates the opportunity to comment on this draft guidance, and especially appreciates the attention to and incorporation of many of our comments on the previous HCV guidances. In general, the guidance is well written and easier to follow. The reorganization of material and the addition of notes, which explain, give rationales, and provide examples are very helpful, as are the flow charts.

As anticipated, this draft guidance incorporates extension of lookback to include HCV 1.0. This was expected and the requirements are an excellent compromise of science and practicality. However, the committee does have some major concerns about the guidance requirements.

Time Frames

1.) Extension beyond 1988

The draft guidance now contains a totally unexpected new requirement to "identify prior collections extending back indefinitely to the extent that electronic or other readily

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99D-1878

C 15

retrievable records exist." This change is analogous to moving the finish line while the race is still in progress, and after some of the participants have completed the race and gone home.

We urgently request that this new provision be deleted based on the following concerns.

- First, we believe that this requirement will result in an unintended slowing of the present lookback efforts. The current effort is very time consuming for blood collection facilities and hospital transfusion services. The further back in time a search must be conducted, the greater the proportion of recipients deceased or lost to follow-up, and the greater the proportion of record retrieval that will be manual rather than electronic.

  Extending lookback to HCV 1.0 will require even more time and effort than for HCV 2.0/3.0 because of the intense manual effort required. Furthermore, locating and reviewing the actual test results (both initial and repeat reactive) and performing the S/CO calculation is considerably more time consuming than just looking at the final interpretation. We are concerned that extending all lookbacks as far as they can go, which will be the effect of this guidance, will bog the system down with minimal reward in terms of infected recipients identified.

- Second, this requirement will force reopening of many completed lookback cases. This commitment of resources must be done without knowledge of whether the hospital can also search its records that far back. The specific consignee hospital is not identified until after the donor test record has been researched, so even if it is known that a particular hospital does not have records, the blood collection agency must do the initial research. It is highly unlikely that a blood collection agency will find that none of its consignees have such records, so effort involved in initial identification of donor records must proceed even when there is little chance that recipient identification and notification will occur.

  This is an ineffective use of time and resources that could be more usefully applied to completing the process already underway based on the September 1998 guidance and to completing HCV 1.0 lookback. According to the July 1999 progress survey of 171 blood collection facilities, 38 facilities (22%) have completed 25% or less of the required record review and 56 facilities (33%) have completed 25% or less of consignee notifications. In that same survey, only 99 facilities (58%) have completed the record review and only 69 facilities (40%) have completed consignee notification. It is clear that resources should be directed to completing the HCV 2.0/3.0 lookback as currently defined, without diverting resources to expand to indefinite and less productive record review.

- Third, we question the value of extending record review back indefinitely. Inasmuch as retention of transfusion service records was previously required only for 5 years, and given the mortality of transfusion recipients from underlying disease, there is

little value achieved from this extension. The more recent requirement for maintaining records for 10 years and the more recent increased use of computerized record systems do not assist a retrieval of records from over a decade ago. Data from surveys of AABB member institutions last year, and again this year, indicated that fewer than half had records extending far enough back beyond 1988 to make this extension worthwhile, and many who did have records available expressed concerns about the conditions of the records and the ability to obtain the necessary information.

Data on the mortality rate of blood recipients identified for lookback notification has been compiled from the effort to date on HCV 2.0/3.0 retrospective lookback.

In Pittsburgh three tertiary hospitals evaluated 1125 recipients and 603 (54%) were deceased; one Children's hospital evaluated 97 recipients, and 55 (57%) were deceased and; three community hospitals evaluated 108 recipients and 78 (72%) were deceased. The overall mortality rate was 738/1330 or 55%.

This is consistent with data from a Midwest hospital in which the Social Security Death Index indicated that 55 of 113 traceable recipients (49%) were deceased. The final number rose to 63 (57%) as a result of subsequent aggressive recipient notification efforts.

Data from the AABB July progress survey shows that records indicated 4183 of 10088 (42%) of identified recipients were deceased, consistent with the CJD Lookback Study being conducted by the National Blood Data Resource Center in which data through June 1999 shows that of 283 identified recipients, 158 or 56% were deceased.

The Committee also asked that same Midwest hospital to provide data on the effectiveness of lookback. This general hospital with a large cardiac surgery program, identified 141 components that required recipient tracing and located 113 records in which transfusion had occurred. As referenced above, 55 recipients were known to be deceased and 58 notifications were sent out. Out of 58 notifications sent out, 43 recipients were located. Three were spouses/children notifying the hospital that the recipient was deceased and the other 40 were tested. Of the 40 that were tested, 3 tested positive, with one of them already being aware of the positive test results. Thus the lookback objective of identifying transfused recipients who do not know of their infection, was successful in only 2 cases out of 141 potential cases.

The Committee believes that this is a typical scenario, and that it is unreasonable to extend the lookback beyond the current time frame. As the records get older, the yield is expected to be even less.

- The Advisory Committee on Blood Safety and Availability (Advisory Committee) understood the incrementally smaller returns to be expected as the process was extended further back and thus recommended that the initial program of targeted lookback extend only to 1988 pending a review of the effectiveness of the initial

effort. The Advisory Committee has not stated a different position, and we believe it would be wise to continue to comply with their recommendation.

The Interorganizational HCV Lookback Committee reminds FDA that targeted lookback was intended to be conducted in tandem with a CDC effort to inform the general public that anyone transfused prior to 1992 (or with behavioral risks for HCV infection) should be tested for HCV. We believe that mechanism will be more effective in achieving the underlying public health objectives of lookback and can be done in a more timely manner than extension of the targeted lookback beyond 1988.

It is understood that the CDC's generalized lookback effort will not reach all potentially infected individuals with a message that prompts them to seek treatment and testing. The experience of the Hoxworth Blood Center in Cincinnati with such a program shortly after the implementation of anti-HCV testing resulted in the testing of only about 5% of the target audience. (Transfusion 1990;30:759-61), and the response rate is no greater when targeted lookback efforts are utilized.

A report of the results of the targeted HCV lookback effort in Milwaukee illustrated that less than 3% of lookbacks resulted in the recipient being tested. (Transfusion 1998;38:4S) Even when the target infection is HIV, with attendant greater public concern, only about 4% of recipients in the San Francisco area receiving a letter urging them to be tested following receipt of a higher-risk unit sought HIV testing. (Transfusion 1991;31:655-61.) Therefore, while the Committee understands the importance of advising potentially infected transfusion recipients of their (increased) risk, it is questionable whether a targeted lookback will provide a greater yield than a generalized one. Consequently, the Committee believes that as the logistic obstacles in lengthening the lookback period increase, there is even greater reason to rely on the generalized lookback.

2.) Begin 1.0 lookback before completion of 2.0/3.0

We request that 1.0 consignee notification be required to begin by May 1, 2000 and be completed by May 1, 2001. Transfusion Services should have one year following notification to complete recipient notification and must have completed it by May 1, 2001.

As stated earlier in these comments, we believe the concept of 1.0 lookback is acceptable, but we are concerned about trying to complete it during the same time frame in which we are trying to complete lookback already underway for 2.0/3.0. If there is a significant public health utility to targeted HCV lookback, it resides in the identification of more recently transfused patients. Completion of the HCV 2.0/3.0 lookback must not be impeded by the new guidance.

3.) Prospective lookback

The Committee requests that a rolling ten years become the required time frame for all new prospective lookbacks.

If 1988 is retained as the time frame, then in each succeeding year, the number of years for which records must be reviewed will continue to increase. Since the new requirement is to maintain records for ten years, it is more appropriate to adopt a time frame for lookback that is consistent with the ten years in which transfusion records are expected to be available.

4.) Prospective lookback recipient notification

The Committee requests that the 12 week time frame for prospective lookback recipient notification be reconsidered.

The Committee has determined that twelve weeks is insufficient time in some cases in which to contact recipients for prospective lookback, particularly for those hospitals that do not have computerized records. It is frequently necessary to obtain the address from the chart, and because of hospital policies, it is sometimes necessary to make several different requests before you can obtain the chart with the necessary information. It is also necessary to allow some time for a response before sending out a second and/or third notification. There is not the same urgency to notify these recipients, as there is for notification about exposure to HIV where early intervention is essential. For HCV, there is minimal information to suggest that early intervention is beneficial. Also, we point out that it will be even more difficult to meet the 12 week notification limit if the lookback is extended beyond 1988, as these older charts will take even longer to obtain.

5.) Quarantine

The Committee would like to reiterate its position that 3 calendar days is an unrealistic expectation for identification and quarantine of prior collections and notification of consignees to quarantine prior collections whenever a donor tests repeatedly reactive. **We continue to support changing this time to 7 days as it was in the July 1996 memorandum.** However, failing that, we request that the wording be changed to 3 working days.

Additional concerns

1.) Autologous donor notification

We request deletion of "NOTE: FDA recommends that blood establishments notify the physicians of autologous donors of the donor's repeatedly reactive test results and supplemental test results, when applicable, for the purpose of medical follow-up and counseling." This note appears in section III, 1, C and III, 2, B.

We believe it is unnecessary to include autologous donors in the notification efforts. It has been standard practice to notify the patient's physician of the repeatedly reactive HCV test result at the time the autologous unit was collected as required in the FDA memo to all registered blood establishments on September 11, 1991 titled "Disposition of Blood Products Intended for Autologous Use That Test Repeatedly Reactive for Anti HCV." This memo also requires collection facilities to indefinitely defer these donors for homologous (allogeneic) donation, so the donor will also have been notified of the HCV test result. Thus additional lookback notification is unwarranted.

2.) Physician identification

We request that the wording in Section III, 4, b be changed to require identification of either the patient's physician of record or the physician responsible for the transfusion order.

Section III, 4 Notification of Transfusion Recipients, part b, requires identification of both the patient's physician of record and the physician responsible for the transfusion order. In part c (i) and (ii) the requirement is to notify the physician of record or the physician that ordered the blood. It is unnecessary to identify both. It should be noted that the ordering physician may not be specifically identified, even in the chart. (For example, requests from the operating room could be considered as emanating from the surgeon or the anesthesiologist – or both – but the precise identification of the requestor is usually not captured.) Furthermore, in teaching institutions, the ordering physician is almost always a house officer who almost certainly, at the time of lookback, is no longer at the institution and who will certainly not be involved in the notification and follow-up of the patient. This new requirement, as proposed, adds significant additional work for no additional patient benefit.

Minor Inconsistencies

There are some minor inconsistencies that we would like to bring to your attention. Throughout the document the term "are at increased risk of transmitting HCV" has been substituted for "may have contained HCV" which was used in the previous guidance. However, Section III, 4 Notification of Transfusion Recipients, introductory paragraph and part c, uses the term "potentially contained HCV", but section e and f uses the terminology "increased risk of transmitting HCV."

Section III, 2, A specifies "donations of blood and blood components intended for transfusion." Section III, 3, A does not include this specification.

Section III, 2, A lists three exceptions, but Section III, 3, A has only two exceptions. We believe that exception 1) "There is no recommendation for quarantine of Source Plasma or Recovered Plasma based on retrospective review of records because few if any unpooled prior collections exist" should be added to Section 3A.

Once again, the Interorganizational HCV Lookback Committee appreciates the opportunity to comment on the draft HCV guidance. The committee is available to assist the FDA in any way. Any question or comments for the committee should be directed to Kay Gregory, AABB Director Regulatory Affairs at 301-215-6522 or kayg@aabb.org.

Yours truly,

Ramona Walker

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Chair, HCV Lookback Committee